

A marked up version of the amendments to the specification and the above claims is enclosed herewith.

REMARKS

The applicants appreciate the Examiner's thorough examination of the application and request reexamination and reconsideration of the application in view of the preceding amendments and the following remarks.

The applicants appreciate and thank the Examiner for allowing claims 28-41, 43 and 44.

The Examiner rejects claim 28 because of the informality that the bond between "C" and the "X" is askew. As shown above, under AMENDMENT C, the applicants have amended claim 28 to now properly show the bond between the "C" and "X".

The Examiner has indicated that in claim 42, line 2, "said bound compounds" should read "--said bound compound--". As shown above, the applicants have amended "said bound compounds" in claim 2 to now recite "said bound compound".

The Examiner requests that claim 5 be canceled because as submitted the claim does not further limit claim 28 as SEQ ID NO:2 of claim 5 has been incorporated into claim 28. Accordingly, as shown above, claim 5 has been cancelled.

The Examiner indicates that claims 2 and 4-8 are dependent upon canceled claims. As shown above, the applicants have canceled claims 2 and 4-8. Accordingly, the Examiner's rejection of these claims is now moot.

The Examiner rejects claims 6 and 8 under 35 U.S.C. §112 second paragraph as being indefinite. Because the applicants have canceled claims 6 and 8, the Examiner's rejection of

these claims is moot.


The Examiner indicates that claim 2 and 4-9 would be allowable if they depend upon claim 28. As shown above under AMENDMENT C, former claim 2 has been added as new claim 45, former claim 4 has been added as new claim 46, and former claims 6-9 have been added as new claims 47-50. New claims 45-50 all depend from claim 28. Accordingly, new claims 45-50 are allowable.

The applicants have also discovered that the amendment filed September 6, 2002 incorrectly amended the replacement of BODIPY[®] with the chemical name 4,4-difluoro-4-bora-3a-diaza-s-indacene instead of the correct chemical name 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene. Accordingly, the applicants have amended the specification at pages 4 and 13 and claim 35 as shown above to replace the chemical name of BODIPY[®] with 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene.

Each of the Examiner's rejections has been addressed or traversed. Accordingly, it is respectfully submitted that the application is in condition for allowance. Early and favorable action is respectfully requested.

If for any reason this Response is found to be incomplete, or if at any time it appears that a telephone conference with counsel would help advance prosecution, please telephone the undersigned or his associates, collect in Waltham, Massachusetts, at (781) 890-5678.

Respectfully submitted,



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Marked Up Claims and Specification

The paragraph beginning on page 4, line 6:

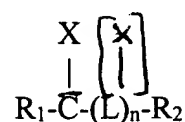
In other preferred embodiments, the light-emitting moiety (R_1) is selected from the group including [4,4-difluoro-4-bora-3a-diaza-s-indacene] 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene, fluorescein, fluorosien isothiocyanate (FITC), Texas red, phycoerythrin, rhodamine, carboxytetramethylrhodamine, indopyras dyes, Cascade blue, coumarins, nitrobenzo-2-oxa-diazole (NBD), Lucifer Yellow, propidium iodide, CY3, CY5, CY9, dinitrophenol (DNP), lanthanide cryptates, lanthanide chelates, non-fluorescent dialdehydes (OPA, NDA, ADA, ATTOTAG reagents from Molecular Probes) which react with primary amines (N-term lys) in the presence of a nucleophile (i.e. CN⁻) to form fluorescent isoindoles, dansyl dyes fluorescamine and dabcyl chloride, 5-((((2-iodoacetyl)amino)ethyl)amino)naphthalene-1-sulfonic acid, long lifetime dyes comprised of metal-ligand complexes (MLC) which consist of a metal center (Ru, Re, Os) and organic or inorganic ligands complexed to the metal such as such as $[\text{Ru}(\text{bpy})_3]^{2+}$ and $[\text{Ru}(\text{bpy})_2(\text{dcbpy})]$, and the like and derivatives thereof. The light-emitting moiety can be attached to the peptide by reaction of a reactive side group (of the light-emitting moiety) with the N-terminal amino acid of bombesin-like peptide. Suitable reactive side groups include, by way of example only, indoacetamide, maleimide, isothiocyanate, succinimidyl ester, sulfonyl halide, aldehydes, glyoxal, hydrazine and derivatives thereof.

The paragraph beginning on page 13, line 19:

In general, any dye, porphyrin, fluorophore, or other light-emitting molecule may be

complexed with the bombesin-like peptide. In preferred embodiments, the light-emitting moiety is selected from the group including [4,4-difluoro-4-bora-3a-diaza-s-indacene] 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene, fluorescein, FITC, Texas red, phycoerythrin, rhodamine, carboxytetra-methylrhodamine, indopyras dyes, Cascade blue, coumarins, NBD, Lucifer Yellow, propidium iodide, CY3, CY5, and CY9, dinitrophenol (DNP), lanthanide cryptates, lanthanide chelates, non-fluorescent dialdehydes (OPA, NDA, ADA, ATTOTAG reagents from Molecular Probes) which react with primary amines (N-term lysine in the presence of a nucleophile (i.e. CN⁻) to form fluorescent isoindoles, dansyl dyes, fluorescamine and dabcyl chloride, 5-((((2-iodoacetyl)amino)ethyl)amino)naphthalene-1-sulfonic acid, long lifetime dyes comprised of metal-ligand complexes (MLC) which consist of a metal center (Ru, Re, Os) and organic or inorganic ligands complexed to the metal such as such as [Ru(bpy)₃]²⁺ and [Ru(bpy)₂(dcbpy)], and the like and derivatives thereof. The synthesis and structures of several dyes which may be used are described in U.S. Patents 5,248,782; 5,274,113; and, 5,187,288, the contents of which are incorporated herein by reference. Other light-emitting moieties used in labeling or other applications may be attached to the peptide. For example, suitable light-emitting moieties are described in “*Handbook of Fluorescent Probes and Research Chemicals – 5th Edition*” by Richard P. Haugland 1994; and “Design and Application of Indicator Dyes”, *Noninvasive Techniques in Cell Biology*: 1-20 by Richard P. Haugland et al., Wiley-Liss Inc. (1990), the contents of each of which is incorporated herein by reference.

28. (Once amended) A compound of the formula:



wherein R₁ is a light-emitting moiety and R₂ is a bombesin-like peptide, fragment, derivative or analog thereof, wherein R₂ is comprised of Val-Pro-Leu-Pro-Ala-Gly-Gly-Gly-Thr-Val-Leu-Thr-Lys-Met-Tyr-Pro-Arg-Gly-Asn-His-Trp-Ala-Val-Gly-His-Leu-Met (SEQ ID NO:2), and L is a linker moiety,

wherein n is 1 or 0, and (C-X) is selected from the group consisting of C=O, C=S, CH(OH), C=C=O, C=NH, CH₂, CH(OR) DH(NR), CH(R), CR₃R₄, and C(OR₃)OR₄ where R, R₃, and R₄ are alkyl moieties or substituted alkyl moieties, and

wherein (L)_n—R₂ is linked to (C-X) at L or at an amino acid position selected such that the compound exhibits substantial biological activity in the presence of a receptor having affinity for bombesin-like peptides, wherein said compound exhibits substantial biological activity in the presence of a receptor having affinity for bombesin-like peptides.

35. (Once amended) The compound of claim 1, wherein said light-emitting moiety is selected from the group consisting of [4,4-difluoro-4-bora-3a-diaza-s-indacene] 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene, fluorescein, FITC, Texas red, phycoerythrin, rhodamine, carboxytetra-methylrhodamine, indopyras dyes, Cascade blue, coumarins, NBD, Lucifer Yellow, propidium iodide, dinitrophenol (DNP), lanthanide cryptates, lanthanide chelates, non-fluorescent dialdehydes which react with primary amines to form fluorescent isoindoles, dansyl, fluorescamine and dabcyl chloride, 5-(((2-iodoacetyl)

amino)ethyl)amino)naphthalene-1-sulfonic acid, long lifetime dyes comprised of metal-ligand complexes (MLC) and derivatives thereof.

42. (Once amended) A method for imaging cell receptor sites comprising contacting candidate cell receptor sites with a compound of claim 28, and detecting said bound [compounds] compound as an indication of said cell receptor sites.